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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/756,411	01/08/2001	Franco Lori	NIH061.1CP1C2	5460

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EXAMINER	
CRANE, LAWRENCE E	
ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 09/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/756,411	LORI ET AL.
	Examiner	Art Unit
	L. E. Crane	1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 08/26/04 (responce & declaration).
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 21-30 is/are pending in the application.
 - 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 21-30 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 08 January 2001 is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) Notice of Informal Patent Application (PTO-152)
- 6) Other: _____

No claims have been cancelled, no claims have been amended, the disclosure has not been amended, and no new claims have been added as per the response filed August 26, 2004. A declaration by applicant Lori including references filed August 26, 2004 has been received. No additional Information Disclosure Statements or declarations have been filed as of the date of this Office action. The additional references supplied by applicant Lori have been made of record on an updated PTO-892.

Claims 21-30 remain in the case.

Claims 21-30 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims 21-30 are directed to pairs of compounds, the specific chemical identities of which either have not been specified or have been only specified in part, and are therefore claimed more broadly than is supportable by the instant disclosed exemplification.

Applicant's arguments filed August 26, 2004 have been fully considered but they are not persuasive.

Applicant Lori has supplied a brief declaration accompanied by two references now cited of record as PTO-892 VC (**Sumpter et al.**) and WC (**Palmer et al.**). Applicant and applicant's representative argue that the disclosure of these two patents support the breadth of the instant claims. Examiner respectfully disagrees. The instant application and its parent and related applications are based on a single report of anti-HIV activity (hydroxyurea + ddI in certain proportions) and, although additional combinations have been allowed (**Lori et al. '390**, PTO-892 ref. J), there is no data from applicant or any other source to confirm the biological activity of the combinations listed in the claims of the '390 patent. Therefore, there is no data to support extrapolation of any kind to other possible combinations. Applicant argues, citing the previously filed declaration of interested party Vila that the choice of test protocol (quiescent or activated) is not a determinative factor, and that the Office must accept as "fact" this assertion of opinion in the absence of a convincing factual showing that the opinion of declarant Vila is anything more than speculation. Examiner has again carefully

reviewed the Vila declaration and does not agree with the conclusions proposed therein because Vila has only presented opinion, but has not presented data to support his conclusion that the failure of the activated test to exclude the AZT + hydroxyurea combination is appropriately ignored as an outlier or is otherwise explainable.

Applicant argues that *Ex parte Balzarini* only requires a “reasonably predictive” standard and therefore, in light of the Vila declaration, that the data from the Gallo/Lori line of applications is admissible in support of the assertion that extrapolation is appropriate. Again Examiner respectfully disagrees because applicant has failed to provide the data required to actually support the assertion that applicant had factual reason to know that combinations other than hydroxyurea + dDI were similarly effective at the original filed date. Again Examiner notes that the Vila declaration is opinion which is not adequately supported by facts.

For these reasons, applicant’s assertions have been considered but have not been found sufficient to overcome the instant grounds of rejection.

Claims 21-30 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one of ordinary skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The fundamental issue here is whether practicing the full scope of the instant invention is possible without undue experimentation. As provided for in *In re Wands* (858 F.2d 731, 737; 8 USPQ 2d 1400, 1404 (Fed Cir. 1988) the minimum factors to be considered in determination of whether a conclusion of “undue experimentation” is appropriate are as follows:

- A. The breadth of the claims is difficult to determine because of reliance on functional terminology in claim 21 including the terms “an inhibitor of ribonucleotide reductase” and “an antiviral nucleoside phosphate analog.”
- B. The nature of the invention is limited to the inhibition of replication of a reverse transcriptase dependent virus in any host from a single cell to a complete human host. This encompasses the treatment of HIV in a human host.

C. The state of the prior art is well defined by the extensive list of prior art references in the PTO-892 and PTO-1449 of record. However, the prior art most relevant to the instant claims is limited to the patent and non-patent references from Messrs. Malley and Vila (US 5,521,161 etc.) wherein the only operative embodiment supporting the instant claims is disclosed.

D. The level of one or ordinary skill is low because only a single prior art exemplification is known in the art.

E. The level of predictability in the art is low because of the existence of only a single enabling prior art exemplification (hydroxyurea/ddI) is known in the prior art.

F. The amount of direction provided by the inventor is, with the exception of the known exemplification, all prospective and therefore not useful in determining whether the prior art exemplification is a singular observation or whether analogous phenomena occur with other combinations of active ingredients.

G. The existence of working examples is limited to the single prior art exemplification, the remaining examples all being prospective; i.e. experimentally unsupported.

H. The quantity of experimentation needed to make or use the invention based on the content of the disclosure is deemed to be excessive because of the absence of working examples to provide a proper basis for extrapolation to other combinations of active ingredients. See also *Ex parte Balzarini et al.* 21, USPQ 2d 1892, 1894 (BPAI, 1991) which in its first opinion stands for the proposition that claims directed to medicinal treatments of diseases in highly unpredictable art areas are properly rejected under 35 U.S.C. §112, first paragraph as lacking adequate enablement, in the absence of sufficient test data in support of the efficacy of the alleged treatment (MPEP at 2107.03 (p. 2100-44, col. 2, in the August, 2001 revision)).

Applicant's arguments filed August 26, 2004 have been fully considered but they are not persuasive.

Applicant is referred to the response to arguments following the previous rejection.

Applicant argues that the burden of experimentation is not undue because one of ordinary skill would find the instant disclosure “reasonably predictive,” in spite of the absence of factual basis for this conclusion. Examiner refers applicant to *Brenner v. Manson*, 148 USPQ 689 (S. Ct., 1966) at p. 696, column 1, wherein it is stated that “[A] patent is not a hunting license. It is not a reward for the search, but compensation for its successful completion.” Applicant has proposed extrapolation wherein the signposts are functional terms which provide insufficient guidance concerning which members of one of the two generic classes work and which do not in combination with individual members of the second class. This level of guidance is deemed to be insufficient because it is only an invitation to experiment or “a hunting license” as suggested by *Brenner*. Therefore, the instant grounds of rejection have been maintained.

Claims 21-30 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In each of claims 21-30 one or both of the active ingredients have not been specified with other than with functional language, and therefore each noted claim lacks properly defined metes and bounds because the ordinary practitioner cannot determine what is included or excluded, or what was included or excluded at the time of filing.

Applicant’s arguments filed August 26, 2004 have been fully considered but they are not persuasive.

Applicant argues that the noted terms “are as accurate as the subject matter permits, such components of a mixture being undefinable by ‘chicken wire’ structural formulas known to organic chemists.” Examiner respectfully disagrees because applicant has, by the statement quoted, only acknowledged a failure of imagination coupled with an absence of factual basis for devising the appropriate structural representations for the generic classes implied by the functional terms noted in the rejection of record. Examiner also refers applicant to any competent text in biochemistry (Biochemistry by Lehninger, etc.) wherein “chicken wire” formulas litter many pages of the text and must be understood in order to follow the explanations in the text.

The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy

reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam*, 686 F. 2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir 1985); and *In re Goodman*, 29 USPQ 2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. §1.78(d).

Effective January 1, 1994, a registered attorney or agent or record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R. §3.73(b).

Applicant's arguments filed October 8, 2003 have been fully considered but they are not persuasive.

Applicant has acknowledged the possible appropriateness of the instant rejection has not provided an appropriate terminal disclaimer.

Claims 21-30 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12-22 of U.S. Patent No. 6,046,175 (PTO-892 ref. H). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed to a binary composition which includes two active ingredients generically defined in a manner which includes the subject matter previously claimed.

Applicant's arguments filed August 26, 2004 have been fully considered but they are not persuasive.

Applicant has acknowledged the possible appropriateness of the instant rejection has not provided an appropriate terminal disclaimer.

Claims 21-30 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3-8 of U.S. Patent No. 6,194,390 (PTO-

892 ref. J). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed to a method of treating HIV in a human host wherein the active ingredients are defined generically in a manner which includes the subject matter of the previously patented claims.

Applicant's arguments filed August 26, 2004 have been fully considered but they are not persuasive.

Applicant has acknowledged the possible appropriateness of the instant rejection has not provided an appropriate terminal disclaimer.

Claims 21-28 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 5,521,161 (PTO-892 ref. E). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed to a method of treating HIV in a human host wherein the active ingredients are defined generically in a manner which includes the subject matter of the previously patented claims.

Applicant's arguments filed August 26, 2004 have been fully considered but they are not persuasive.

Applicant has acknowledged the possible appropriateness of the instant rejection has not provided an appropriate terminal disclaimer.

Claims 21-30 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 5,736,527 (PTO-892 ref. G). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed to a method of treating HIV in a human host wherein the active ingredients are defined generically in a manner which includes the subject matter of the previously patented claims.

Applicant's arguments filed August 26, 2004 have been fully considered but they are not persuasive.

Applicant has acknowledged the possible appropriateness of the instant rejection has not provided an appropriate terminal disclaimer.

Claims 21-30 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6-8 of U.S. Patent No. 6,093,702 (PTO-892 ref. K). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed to a binary composition which includes two active ingredients generically defined in a manner which includes the subject matter previously claimed.

Applicant's arguments filed August 26, 2004 have been fully considered but they are not persuasive.

Applicant has acknowledged the possible appropriateness of the instant rejection has not provided an appropriate terminal disclaimer.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

"A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent."

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States."

Claims 21-26 are rejected under 35 U.S.C. §102(b) as being anticipated by **Palmer et al.** (PTO-892 ref. WC).

Applicant is referred to the abstract and to page 2048, column 2, wherein the synergistic anti-HIV effects of hydroxyurea with ddI and the nucleoside analogue "PMEA" are specifically noted.

Applicant's arguments with respect to claims 21-30 have been considered but are deemed to be moot in view of the new grounds of rejection.

Papers related to this application may be submitted to Group 1600 via facsimile transmission(FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX

(unofficially) directly to Examiner's computer is 571-273-0651. The telephone number for sending an Official FAX to the PTO is 703-872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson, can be reached at **571-272-0661**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

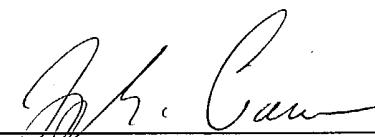
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